Mass Spectra of Substituted Δ^2-1,2,4-Oxadiazolines. II (1-3)

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5,5-Pentamethylene-3-(phenyl or *para*-substituted-phenyl)-Δ^2-1,2,4-oxadiazolines, **1a-e**, were examined by electron-impact mass spectrometry. Defocussed metastable ion detections confirmed the formation of certain daughter fragments from the mother ions. The exact mass measurements helped to make the correct assignment of various species. We conclude that it is the spiro arrangement which caused such a dramatic change in the decomposition pattern. Several new fragmentation pathways have been found in the present studies. Out of five oxadiazolines prepared for the present work, three (**1b,d,e**) are new.

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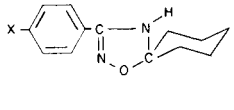
Introduction.

So far, two reports (3,4) have appeared on mass spectral studies of Δ^2-1,2,4-oxadiazolines. In the first series of compounds (4), all the three positions, *viz*, 3,4 and 5 of the heterocyclic ring were substituted and in the second series (3) only 3 and 5 positions had substituents. In the latter case (3), the methyl function at C-3 was replaced by a phenyl or *p*-substituted phenyl group whereas an ethyl in place of phenyl group was put at C-5. It was shown that interchanging the groups between C-3 and C-5 greatly modified the fragmentation pathways. However, in all the compounds previously studied (3,4), there was only one substituent in the 5 position.

To our knowledge the 3,5,5-trisubstituted Δ^2-1,2,4-oxadiazolines have not been investigated by mass spectrometry. It was, therefore, of interest to examine the electron-impact effects on 3-phenyl (or *p*-substituted phenyl)-5,5-pentamethylene-Δ^2-1,2,4-oxadiazolines, 1a-e (Figure 1) since these also represent spiro system. The substances, 1a-e, differ from the recently reported ones (3) principally in their substitution at C-5. We have found that the introduction of 5,5-pentamethylene function caused drastic changes in fragmentation. The results and discussion below will show the role of spiro arrangement in modifying the decomposition mode completely.



1a, X = H
b, X = CH_3
c, X = Cl
d, X = Br
e, X = NO_2

Fig. 1

Results and Discussion.

The compound **1a** (Figure 2) provided the molecular ion *a* at m/e 216. This species then loses the hydroxyl radical to afford the fragment *c* in a relative abundance of 2%. The other four substances, **1b-e**, also show the loss of .ÖH radical from $M^{+\cdot}$ (See Table I). Species *a* is in equilibrium with *b*. The loss of ethyl and propyl radicals occurred from ion *b* to give the daughter fragments *d* and *g* respectively. Ion 187, an even electron ion, provides an odd electron ion at m/e 160. The fragment *g* breaks to give a species with mass 55, the base peak in the spectrum. The direct analysis of daughter ions (d.a.d.i.) confirmed these assignments. Scheme I shows the various fragmentation modes which have been observed for the first time in Δ^2-1,2,4-oxadiazoline series. D.a.d.i. established the origin of species *j* from the precursor ion 173. The exact mass measurement had the composition $C_7H_7N_2^+$. A mechanism of formation of this fragment is proposed, which involves a six-membered transition state for the transfer of a hydride ion to the positive nitrogen followed by the ejection of C_3H_3O molecule from *h'* to provide the fragment *j* (Scheme II).

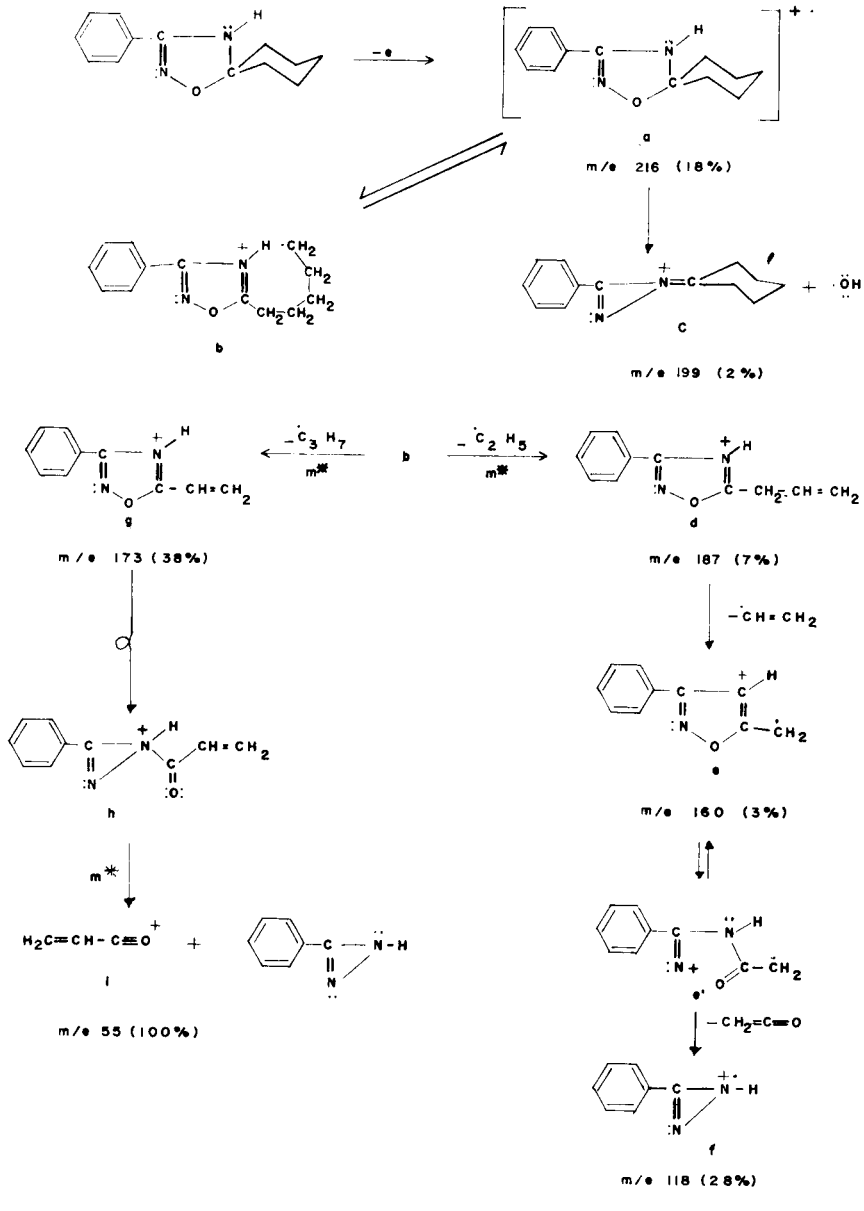
The relative abundance of m/e 119 was about 7% in 1a. The percentage of the corresponding ion in 1b increased indicating the stabilization of ion *j* by the +I effect of CH_3 group at para position of phenyl ring. Replacement of methyl function by Cl, Br or NO_2 have the expected reverse effect and therefore no ions corresponding to *j* were observed in 1c-e. Table I lists the relative abundance of various ions.

The most interesting ion appeared at m/e 118. It has been found in 1a in a relative abundance of 28% and has originated from species *e*. The exact mass measurement shows it to compose of $C_7H_6N_2^{+\cdot}$. The relative abundance of the corresponding ion in 1b (Figure 3) increased (44%), whereas in **1c-e** (Figures 4-6) these were comparatively in smaller abundance. A structure of this fragment is proposed (Scheme III)

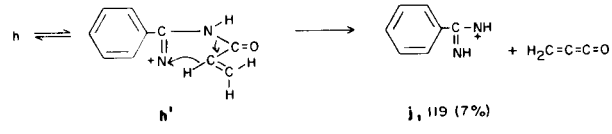
It is fascinating to note that *k* rearranges to *l* and then decomposes to *m* and *n*. Also *l* may produce the species *n*. D.a.d.i. helped to establish this. The species *m* and *n* were not found in **1c**.

The d.a.d.i. spectra of **1c** showed that the ion 152 after rearrangement breaks up to provide two fragments - one

0022-152X/81/010095-06$02.25



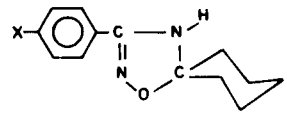
Scheme I



Scheme II

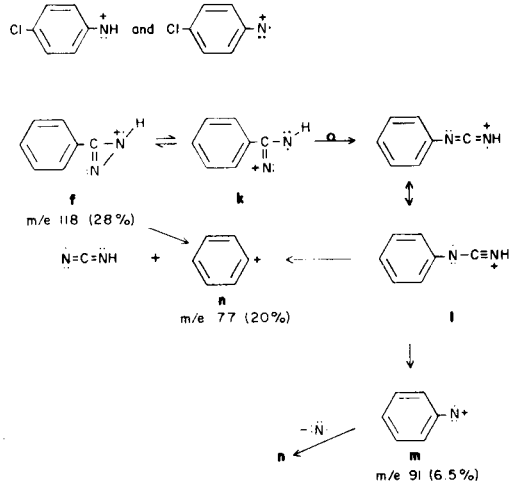
Table I

Relative abundance of ions of Δ^2-1,2,4-oxadiazolines



X = H		X = Me		X = Cl		X = Br		X = NO_2	
m/e	R. I. %	m/e	R. I. %	m/e	R. I. %	m/e	R. I. %	m/e	R. I. %
216	18.0	230	27.0	250	17.0	294	15.0	261	15.0
199	2.0	213	2.5	233	2.0	277	1.0	244	2.0
187	7.0	201	4.0	221	6.0	265	5.0	232	7.0
173	38.0	187	40.0	207	40.0	251	25.0	218	43.0
160	3.0	174	4.0	194	3.0	238	1.0	205	3.0
119	7.0	133	22.0	153	4.0	197	-	164	-
118	28.0	132	44.0	152	17.0	196	14.0	163	7.0
104	11.0	118	18.0	138	5.0	182	1.5	149	4.0
103	8.5	117	12.0	137	10.0	181	4.5	148	-
92	<0.5	106	<1.0	126	-	170	-	137	<0.5
91	6.5	105	5.0	125	4.0	169	2.0	136	-
77	20.0	91	27.0	111	3.5	155	1.5	122	-
55	100.0	55	100.0	55	100.0	55	100.0	55	100.0
51	9.0	51	5.0	51	3.6	51	5.0	51	3.0
41	25.0	41	33.0	41	23.0	41	28.0	41	42.0

at m/e 126 and the other at m/e 125. The former and the latter are due to



Scheme III

The rearrangement of *k* to *l* was not observed before in Δ^2-1,2,4-oxadiazolines. Previously, (3), a similar type of rearrangement was reported from the ion 119.

In summary, we have found that it is the spiro arrangement which caused major alteration in decomposition pattern. For example, in 5-ethyl-3-(phenyl or *p*-substituted phenyl)-Δ^2-1,2,4-oxadiazolines (3), the base peak was at m/e 119 or its corresponding ion whereas in the present study, this species represents a small percentage. In the current series, the base peak is at m/e 55. The other major point to note is the appearance of ion *k* or *l* in 1a-e. This was almost absent in the previous study (3). Also, the loss of $\cdot\ddot{O}H$ from $M^{+\cdot}$ is common in all the five compounds reported in this paper. All the observations suggest a major change in fragmentation pathways due to the spiro arrangement.

Condensation of the desired benzamidoxime (5) with cyclohexanone in presence of acetic acid afforded Δ^2-1,2,4-oxadiazolines, 1a-e. Compound 1a was synthesized according to the procedure reported (6) earlier. Compounds 1b-e were prepared by modifying the previous technique (6) although the yields could not be improved. Three oxadiazolines, *viz.*, 1b,d,e are new.

EXPERIMENTAL (8)

Melting points were determined on Thomas Hoover Capillary Melting Point Apparatus (Serie 71) and are uncorrected. Ir spectra were recorded on Perkin-Elmer Infracord spectrophotometer Model 237B. Nmr spectra were measured on Varian A-60 instrument. The solvents used were: deuteriochloroform for **1a-b**, methanol d_4 for **1c**, and DMSO-d_6 for **1d-e** with tetramethylsilane as internal standard. Thin layer chromatography was done on plates coated with Silicagel G (Merck) using chloroform as solvent for development and iodine for the detection of spots.

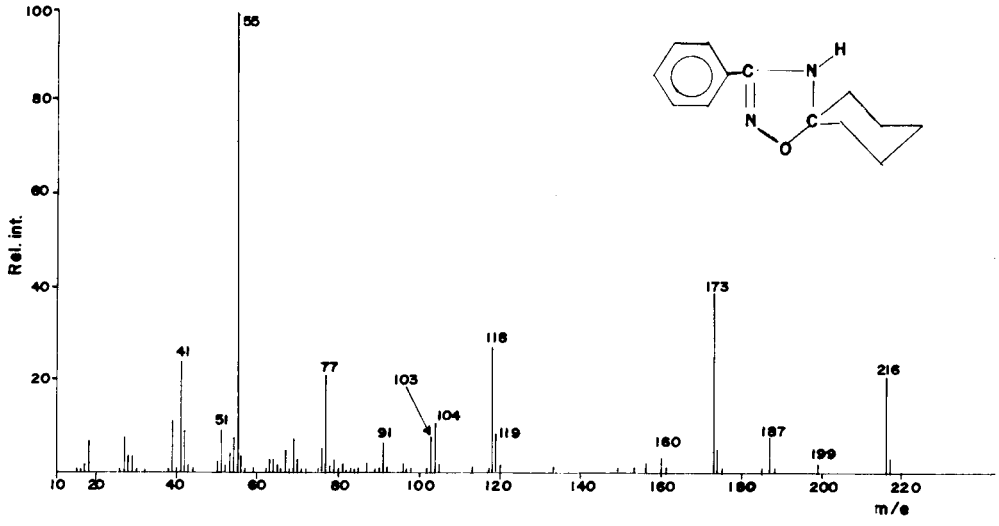


Fig. 2. Mass spectrum of 5,5-pentamethylene-3-phenyl-Δ^2-1,2,4-oxadiazoline.

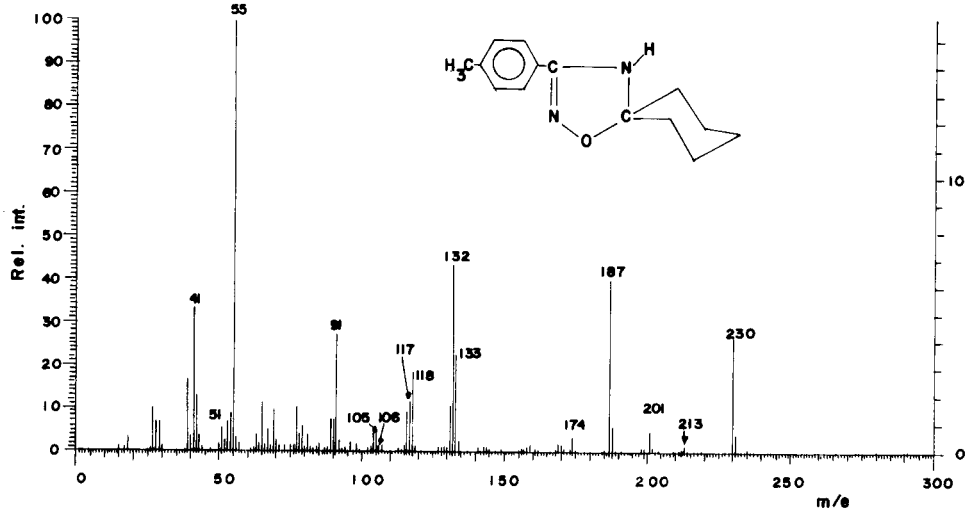


Fig. 3. Mass spectrum of 5,5-Pentamethylene-3-(p-tolyl)-Δ^2-1,2,4-oxadiazoline

The d.a.d.i. measurements, the high resolution and the computer plot of all the compounds were made on Varian MAT CH-5-DF spectrometer coupled with SS100 MS Varian data system. The ionization energy was 70 ev in all cases. The samples were introduced through the direct insertion probe. The temperature of the probe was 100° for compounds 1a and 1b and 160° for substances 1c-e.

5,5-Penetamethylene-3-phenyl-Δ^2-1,2,4-oxadiazoline (**1a**).

This compound was prepared in a similar manner as described (6) earlier.

5,5-Pentamethylene-3-*p*-tolyl-Δ^2-1,2,4-oxadiazoline (**1b**).

p-Tolylamidoxime (0.828 g., 5.52 mmoles), cyclohexanone (10 ml.) glacial acetic acid (20 ml.) and benzene (120 ml.) were refluxed for 6 hours and then cooled. Thin layer chromatography showed two spots with R_f values 0.14 and 0.26. After solvent removal, the residue was chromatographed over 15 g. of Silicagel (Merck) using benzene-chloroform (3:1) as eluent. Fractions containing the fast moving spot were combined and solvent removed to yield 0.52 g. (41%) of crystalline and chromatographically pure **1b**. Recrystallization from chloroform and *n*-hexane gave crystals which melted at 177-178°.

Anal. Calcd. for $C_{14}H_{18}N_2O$: C, 73.04; H, 7.88; N, 12.17. Found: C, 72.81; H, 7.79; N, 12.49.

The slow moving spot was *p*-tolylamidoxime.

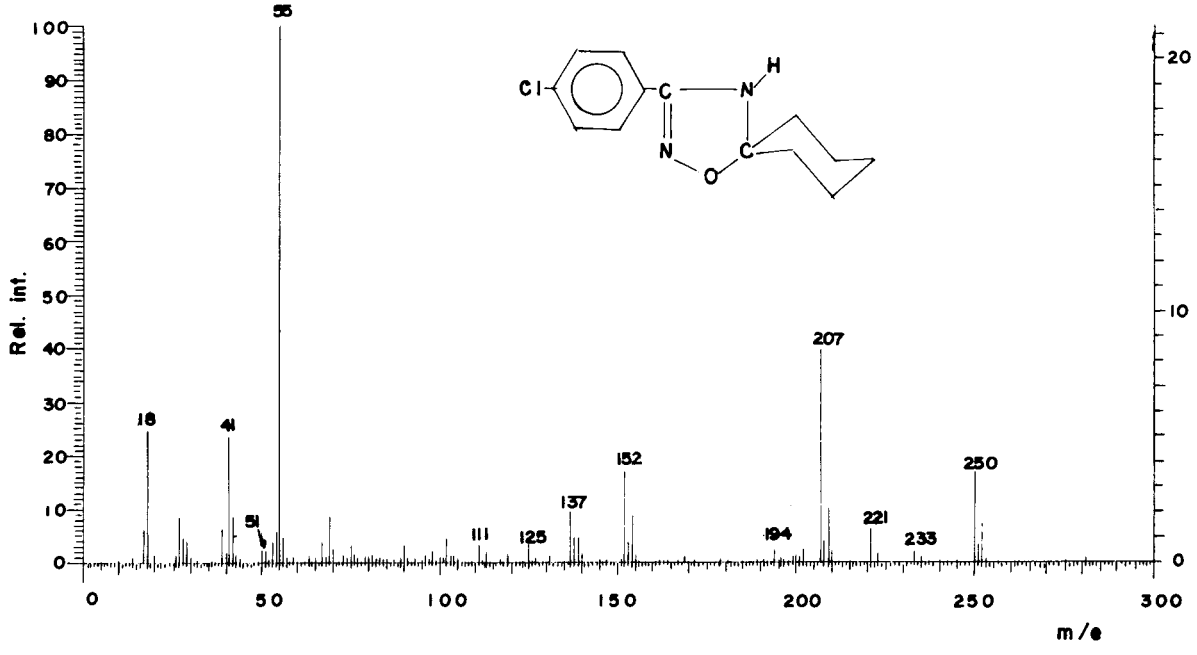


Fig. 4. Mass spectrum of 3-(p-Chlorophenyl)-5,5-pentamethylene-Δ^2-1,2,4-oxadiazoline

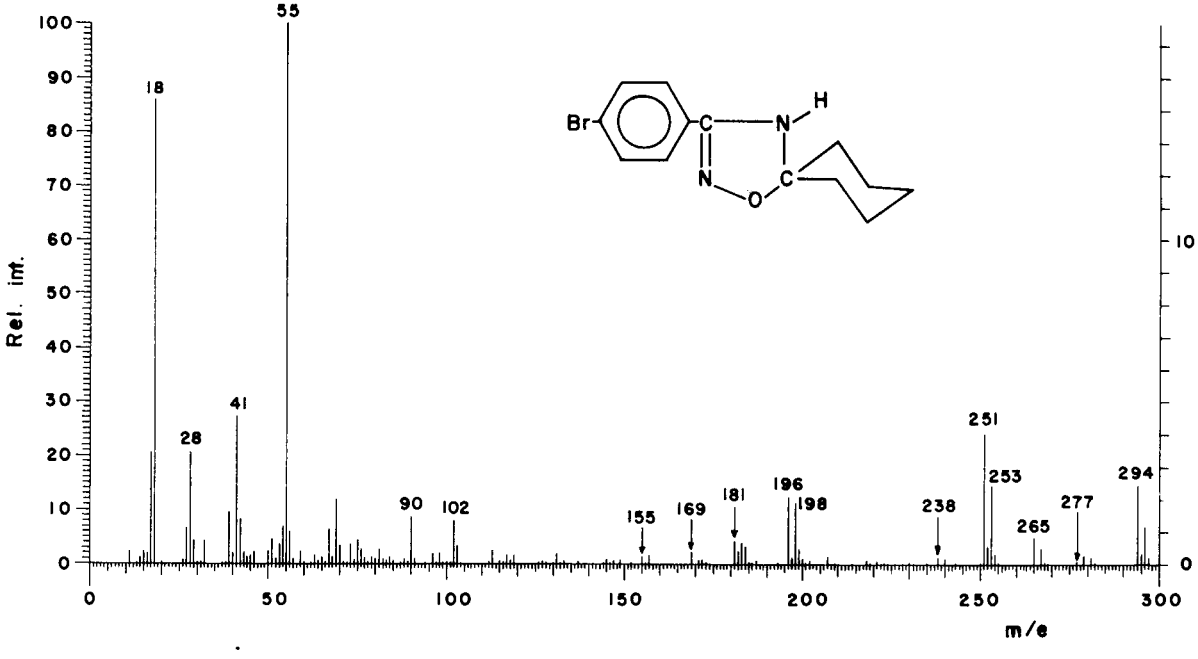


Fig. 5. Mass spectrum of 3-(p-Bromophenyl)-5,5-pentamethylene-Δ^2-1,2,4-oxadiazoline

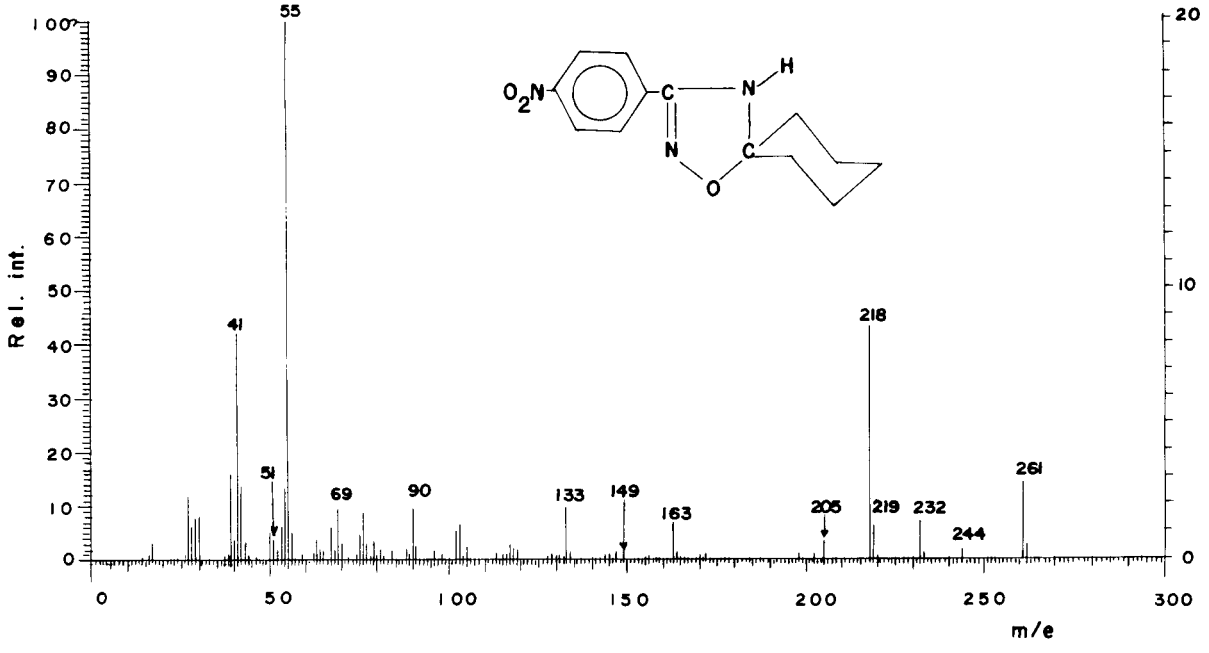


Fig. 6. Mass spectrum of 3-(p-Nitrophenyl)-5,5-pentamethylene-Δ^2 1,2,4-oxadiazoline

3-*p*-Chlorophenyl-5,5-pentamethylene-Δ^2-1,2,4-oxadiazoline (**1c**).

The reaction was performed in the same manner as described for **1b**. After work up and chromatography, a crystalline material was obtained in 14% yield. Recrystallization from chloroform and hexane gave light colorless crystals, m.p. 184-186°; lit. (7) m.p. 208-212°.

Anal. Calcd. for $C_{13}H_{15}ClN_2O$: C, 62.27; H, 6.03; N, 11.17. Found: C, 62.18; H, 6.05; N, 11.18.

The nmr spectrum was consistent with the structure.

3-*p*-Bromophenyl-5,5-pentamethylene-Δ^2-1,2,4-oxadiazoline (**1d**).

The procedure was the same as described above. After column chromatography followed by repeated crystallizations, a colorless compound was obtained from benzene in 30% yield having m.p. 187-188°. The spectral results tallied with the structure **1d**.

Anal. Calcd. for $C_{13}H_{15}BrN_2O$: C, 52.89; H, 5.12; N, 9.49. Found: C, 52.61; H, 5.16; N, 9.62.

3-*p*-Nitrophenyl-5,5-pentamethylene-Δ^2-1,2,4-oxadiazoline (**1e**).

Adopting the above method and starting from *p*-nitrobenzamidoxime, a yellow solid was obtained after work up. Examination of the product on thin layer chromatogram showed it to consist of two spots with R_f values of 0.19 and 0.51. Chromatography on Silicagel using chloroform as solvent first provided compound 1e as yellow crystals. Crystallization from benzene gave 0.2 g. (13.8%) of crystals which shrank at 173° and melted at 177-179° dec. Recrystallization did not alter the melting point.

Anal. Calcd. for $C_{13}H_{15}N_3O_3$: C, 59.77; H, 5.74; N, 16.09. Found: C, 59.56; H, 5.87; N, 16.12.

The R_f value of the slow moving spot was the same as *p*-nitrobenzamidoxime.

Acknowledgment.

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REFERENCES AND NOTES

(1) Taken in part from M.Sc. thesis of Julianna F. C. de Albuquerque, Universidade Federal de Pernambuco, Recife, 1977.

(2) Presented at the 30th annual meeting of Sociedade Brasileira para o Progresso da Ciência (SBPC) in São Paulo on July 11, 1978.

(3) For paper I in this series, see R. M. Srivastava, *Org. Mass Spectrom.*, **13**, 14 (1978).

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(5) F. Eloy and R. Lenaers, *Chem. Rev.*, **62**, 155 (1962) and references therein.

(6) R. M. Srivastava and I. M. Brinn, *J. Org. Chem.*, **42**, 1555 (1977).

(7) C. Ainsworth, W. E. Buting, J. Davenport, M. E. Callender and M. C. McCowen, *J. Med. Chem.*, **10**, 208 (1967).

(8) Elemental analyses were performed by Dr. Riva Moscovici, Instituto de Química, Universidade de São Paulo, São Paulo.